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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/383,318	08/26/99	BELGHUITH K	6004.200-US

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EXAMINER	
SLOBODYANSKY,E	
ART UNIT	**PAPER NUMBER**
1652	9

DATE MAILED: 04/26/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/383,318	Applicant(s) Belghuith et al.
	Examiner Elizabeth Slobodyansky	Group Art Unit 1652

☒ Responsive to communication(s) filed on *Feb 1, 2000*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-22* is/are pending in the application.

Of the above, claim(s) *1-12 and 21* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *13-20 and 22* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: *Tunusia 99.100 filed 5/26/99*.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-12 and 21, drawn to glucose isomerase and a method of making thereof, classified in class 435, subclass 71.1.

II. Claims 13-20 and 22, drawn to a DNA encoding glucose isomerase, a variant thereof, a vector containing said DNA, a cell transformed with said vector and a method for producing of said glucose isomerase, classified in class 435, subclass 233.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are patentably distinct because an enzyme and a DNA are different compounds each with its own chemical structure and function, and they have different utilities. A DNA molecule of invention II is not limited in use to the production of glucose isomerase of invention I and can be used as a hybridization probe, and glucose isomerase of invention I can be obtained by a materially different method such as the chemical synthesis.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their divergent subject matter, fall into

different statutory classes of invention, and are separately classified and searched, restriction for examination purposes as indicated is proper.

During a conversation with Ms. Carol Rozek on January 19, 2000 a provisional election was made with traverse to prosecute the invention of Group II, claims 13-20 and 22. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-12 and 21 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Tunisia on May 26, 1999. It is noted, however, that applicant has not filed a certified copy of the Tunisian application as required by 35 U.S.C. 119(b).

Drawings

The drawings filed concurrently with the application have been objected by Draftsperson, please see the attached PTO-948 form for details.

Claim Objections

Claims 13, 14 and 22 are objected to because of the following informalities: claims 13 and 22 depend from non-elected claim 1. In the interests of compact prosecution, they have been considered as to include all limitations of claim 1.

Claims 13 and 14 recite "amino acids of SEQ ID NO:2" (emphasis added) where it appears amino acid sequence is intended.

Appropriate correction is required.

Specification

The instant disclosure contains sequence disclosure that is encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825. 37 CFR 1.821(d) requires the use of assigned sequence identifier in all instances where the description or claims of a patent application discuss sequences. For example, while Figure 5 shows sequences, there is no reference to sequence identifiers either in the figure or in description thereof; on page 5, line 30; page 37, line 1, a sequence is recited without sequence identifiers.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 13, with dependent claims 15-17, claims 14, 18-20 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 13 and 22 depend from non-elected claim 1. Claim 1(b) is drawn to a variant glucose isomerase having an amino acid sequence of SEQ ID NO:2 comprising a substitution, deletion, and/or insertion of one or more amino acids. Claims 14 and 18-20 recite SEQ ID NO:1 having at least one mutation. There is no limitation on the structural homology. Such mutant and a DNA encoding thereof encompass a great number of molecules, both naturally occurring and synthetic, some of which may not have any structural homology with SEQ ID NOs:2 and 1, respectively. Claim 1(d) recites glucose isomerase having the specific pH and temperature optima. Applicants disclose a single glucose isomerase from *Streptomyces* sp. SK having amino acid

sequence of SEQ ID NO:2, encoded by SEQ ID NO:1 and having properties recited in claim 1(d). Thus, the representative number of species is one. While the art teaches numerous glucose isomerases of various types (for example, Wuxiang et al., Brown et al., cited on form PTO-1449), it teaches no glucose isomerase with the recited properties. The specification does not disclose identifying characteristics which would allow to distinguish a glucose isomerase having the requisite properties from other glucose isomerases. Applicants do not teach modifications of the enzyme structure that would result in retaining the specific glucose isomerase activity of the instant invention. Furthermore, based on the instant disclosure, it is unpredictable which protein structure except SEQ ID NO:1 will impart a glucose isomerase activity to a protein. Thus, a DNA encoding glucose isomerase having the properties recited in claims 13-20 and 22 lacks sufficient written description.

Claim 13, with dependent claims 15-17, claims 14, 18-20 and 22, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA encoding a glucose isomerase from *Streptomyces* sp. SK with the requisite properties or glucose isomerase comprising amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for a DNA encoding glucose isomerase having the requisite properties of unknown primary structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most

nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7)considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

Although the specification teaches a glucose isomerase with the requisite characteristics from *Streptomyces* sp. SK having the amino acid sequence of SEQ ID NO:2, it lacks guidance for a with a glucose isomerase with a different structure having the same properties.

Despite knowledge in the art for the purification of polypeptides and the isolation of DNA molecules, the specification fails to provide guidance regarding characteristics that would allow to distinguish and identify a glucose isomerase of the instant invention. This is because the prior art teaches various glucose isomerases with different structure and physico-chemical and biochemical characteristics, *supra*. Furthermore, it is *a priori* unpredictable as to which species known possess enzymes

with the sequences rendering the requisite properties. Therefore, the breadth of these claims is much larger than the scope enabled by the specification.

The state of the art does not allow the predictability of the properties based on the structure. An amino acid sequence determines the structural and functional properties of an enzyme and knowledge of which sequences can be altered or removed and still result in a requisite enzyme activity is well outside the realm of routine experimentation. One skilled in the art would require guidance as to how to make a sequence that will impart the specific glucose isomerase activity of the invention.

Therefore, one of ordinary skill would require guidance, in order to make and use a glucose isomerase having properties recited in claims 13-20 and 22 other than the glucose isomerase with the requisite characteristics from *Streptomyces* sp. SK having the amino acid sequence of SEQ ID NO:2 in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 recites the mutant nucleic acid sequence encoding SEQ ID NO:2. It is unclear either Applicants intend to claim a degenerate sequence encoding SEQ ID NO:2 or a mutant DNA encoding a sequence different from SEQ ID NO:2.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13-17 and 22 rejected under 35 U.S.C. 102(b) as being anticipated by Belghith et al.

Belghith et al. (form PTO-1449) disclose molecular cloning of glucose isomerase from *Streptomyces* sp. SK, i.e., the enzyme of the instant invention. The glucose isomerase described by Belghith et al. has the same pH and temperature optima as the enzyme of the instant invention (page 554, Figures 1 and 2). They disclose plasmids pBSK1 and pBSK2 carrying the *xylA SK* gene, the gene encoding the enzyme of the instant invention (page 555, 1st column, 2nd and 3rd paragraphs and Figure 3). These plasmids have been expressed in *E. coli*, *ibid*. The *xylA SK* gene inherently has nucleotide sequence of SEQ ID NO:1 which encodes the amino acid sequence of SEQ ID NO:2. Therefore, Belghith et al. anticipate claims 13-17 and 22.

Claims 19 and 20 rejected under 35 U.S.C. 102(b) as being anticipated by Bejar et al.

Bejar et al. (form PTO-1449) disclose the *xylA* genes from *S. violaceoniger* and *S. olivochromogenes* and *E. coli* comprising thereof. The encoded glucose isomerases have 92.5 and 94% identity, respectively, with SEQ ID NO:2. Therefore, Bejar et al. anticipate claims 19 and 20.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Belghith et al.

The teachings of Belghith et al. are outlined above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce a mutant of the *xylA SK* gene using techniques well known in the art. One skilled in the art would have been motivated to produce a mutant in order to study the role of various amino acid residues in the enzyme's function, for example. One skilled in the art would have been motivated to produce a mutant having

95% identity to SEQ ID NO:2 in order to identify the essential residues, given that the sequence from *S. olivochromogenes* has more than 94% identity.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

Elizabeth Slobodyansky, PhD

April 20, 2000